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Andrew Austen Mortlock

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ASTRAZENECA R&D BOSTON
35 GATEHOUSE DRIVE
WALTHAM, MA 02451-1215

EXAMINER

TRUONG, TAMTHOM NGO

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

FINAL ACTION

Applicant's amendment of 1-13-09 has been considered. The amended claim 18 has overcome the previous rejection of 112/2nd paragraph, and thus said rejection is now withdrawn. Claim 3 has been corrected with proper dependency, and the previous objection is also withdrawn. The non-elected species in claim 10 have been deleted, and the previous objection on that claim is withdrawn as well. However, applicant's argument on the previous 103 rejection based on **Mortlock et. al.** (WO'597) in view of **Wang et. al.** (WO'188) is not persuasive, and thus said rejection is maintained herein.

Claims 2, 5, 7, 12-15 and 22 are cancelled.

Claims 16, 17 and 19 are withdrawn.

Claims 1, 3, 4, 6, 8-11, 18, 20, 21 and 23 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 4, 6, 8, 9, 11, 18, 20 and 21 remain rejected under 35 U.S.C. 103(a) as being obvious over **Mortlock et. al.** (WO 01/21597 A1 or WO'597 – cited on IDS) in view of **Wang et. al.** (WO 03/000188 A2 or WO'188 – cited on IDS). A part of said rejection is reiterated as below:

On page 36 of WO'597, Table 14 lists several compounds, among those compounds, compound #331 is relating to a compound of the instant formula (I) with the following substituents:

- i. A is formula (b);
- ii. X is NR^{14} ; R^{14} is hydrogen;
- iii. Y is O; R^4 is a benzyl group;
- iv. R^3 is an alkoxy group;
- v. Z is NR^1R^2 ; $m = 2$;

The disclosed compound can inhibit aurora 2 kinase and treat cancer. However, it differs from the instant compound by not having a *phosphonoxy* group as a substituent on the alkyl groups corresponding to the instant R^1 and R^2 .

Said difference can be overcome by the teaching of Wang et. al. (WO'188). On page 178, Wang claims an aniline-quinazoline compound which has a *phosphonooxy* group as a terminal group of the substituent at the 7-position corresponding to the instant Z variable. Wang's compound can inhibit EGF and treat cancer. Thus, the skilled chemist would have been motivated to add the phosphonooxy group to the substituent at the 7-position of Mortlock's compound because said compound would have been expected to inhibit EGF and treat cancer. Applicant argued that:

There is nothing in Mortlock that suggests alternative compounds are required or desired, and thus nothing that would prompt the skilled artisan to consider modifying with a phosphonooxy group. The skilled artisan would consequently have no reason to consult Wang. As Mortlock does not in itself provide any suggestion or motivation to make the claimed invention and would not cause the skilled person to consult Wang (nor does Wang suggest to the skilled artisan to consult Mortlock), Applicants contend that the standard for a prima facie case of obviousness set out in MPEP 2144.08 has not been satisfied.

Even assuming for the sake of argument that the ordinarily skilled artisan did have reason to consult Wang, Wang does not specifically disclose a phosphonooxy group. Numerous phosphorus containing moieties are contemplated but Applicants cannot find a specific disclosure of phosphonooxy i.e. $-OP(O)(OH)_2$. Of the many compounds disclosed by Wang, none contain a phosphonooxy group. Consequently if the skilled artisan did consult Wang, he would not find aniline-quinazoline compounds bearing a phosphonooxy group (as there are none) and so could not be motivated to modify Mortlock to arrive at the claimed invention.

Response to argument: Although Mortlock does not suggest modifying his quinazoline compounds with a specific phosphonooxy group, his compounds have a combination of substituents that are within the scope of the instant formula (I). In addition, Mortlock's generic

formula (I) also allows for a "prodrug" which usually has an ester group such as "phosphonooxy". Then on page 22, Mortlock defines "prodrug" to include "phosphates" as follows:

Suitable prodrugs of compounds of formula (I) are groups which enhance solubility and include phosphates and sulphates, in particular phosphates as well as alkyl, aryl or aralkyl derivatives thereof such as dibenzylphosphate. The prodrug moiety may be attached at any suitable position in the molecule, for example as a derivative of a hydroxy group, but in particular, may be advantageously present on one or more of groups R^1 , R^2 , R^3 or R^4 , and preferably at R^2 or R^3 .

The teaching of Wang overcomes the deficiency of Mortlock's compounds by disclosing analogous quinazoline compounds on page 178 having a *phosphonooxy* group. Applicant argued that Wang's compounds do not have a *phosphonooxy* group (i.e., $-\text{OP}(\text{O})(\text{OH})_2$), which is attached to the side chain via $-\text{O}-$. However, applicant's species **do not** have a phosphonooxy group, but rather a **phosphate** group (i.e., $-\text{P}(\text{O})(\text{OH})_2$), which is attached to the side chain via $-\text{P}-$ as suggested by Wang. Clearly, the term "phosphonooxy" in the claims must have been meant as "phosphate" as evident by species made.

Therefore, it is maintained that Wang provides a clear motivation to the skilled chemist to modify Mortlock's compounds by adding a phosphate or phosphonooxy group to the side chain because such a group is known in the art to be on a "prodrug".

Therefore, at the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify Mortlock's compound by adding a phosphonooxy or a phosphate group as taught by Wang et. al.

Allowable Subject Matter

Claims 10 and 23 are allowable because they recite species with a side chain having an amino group and a terminal phosphate group which is not taught or fairly suggested by the prior art of record.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

***/Tamthom N. Truong/
Patent Examiner, Art Unit 1624***

***/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624***

5-14-09